PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

Date of mailing (day/month/year) 08 July 1999 (08.07.99)	
International application No. PCT/US98/21276	**Applicant's or agent's file reference** 22000.0086/P
International filing date (day/month/year) 08 October 1998 (08.10.98)	**Priority date** (day/month/year) 10 October 1997 (10.10.97)
Applicant RUBIN, Donald, H. et al	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   10 May 1999 (10.05.99)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Diana Nissen

Telephone No.: (41-22) 338.83.38

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

09/509812

Applicant's or agent's file reference PCT-F30	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP98/04352	International filing date (*day/month/year*) 28 September 1998 (28.09.1998)	Priority date (*day/month/year*) 09 October 1997 (09.10.1997)
International Patent Classification (IPC) or national classification and IPC C07D 295/22		
Applicant FUJISAWA PHARMACEUTICAL CO., LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 05 April 1999 (05.04.1999)	Date of completion of this report 04 January 2000 (04.01.2000)
Name and mailing address of the IPEA/JP Japanese Patent Office, 4-3 Kasumigaseki 3-chome Chiyoda-ku, Tokyo 100-8915, Japan Facsimile No.	Authorized officer Telephone No. (81-3) 3581 1101

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP98/04352

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed

pages _____, as amended (together with any statement under Article 19

pages _____, filed with the demand

pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed

pages _____, filed with the demand

pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP98/04352

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-2	YES
	Claims		NO
Inventive step (IS)	Claims	1-2	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-2	YES
	Claims		NO

2. Citations and explanations

The same reaction as the one in this application or a description that will self-evidently lead to that kind of reaction is not described in any of the documents cited in the international search report. Therefore, the inventions described in this application appear to be novel and to involve an inventive step.

11-H

09/509712 17

PATENT COOPERATION TREATY

PCT

REC'D 01 FEB 2000

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT1028-031/CG	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US98/21276	International filing date *(day/month/year)* 08/10/1998	Priority date *(day/month/year)* 10/10/1997
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant VANDERBILT UNIVERSITY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☒ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10/05/1999	27.01.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer van Heusden, M Telephone No. +49 89 2399 8145

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US98/21276

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-40 as originally filed

Claims, No.:

1-29 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:

☐ the claims, Nos.:

☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

☐ copy of the earlier application whose priority has been claimed.

☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 18, 27-29, as well as claims 1-17, 19-26 insofar as these relate to sequences other than SEQ ID NO:1.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 18, 27-29, as well as claims 1-17, 19-26 insofar as these relate to sequences other than SEQ ID NO:1.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17, 19-26 (insofar as they relate to SEQ ID NO:1)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-17, 19-26 (insofar as they relate to SEQ ID NO:1)
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-16, 24-26
	No:	Claims	17, 19-23 (?)

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Additional remarks to section II:

1. Citations
   The documents mentioned in this IPER are numbered as in the International Search Report (ISR), i.e. D1 corresponds to the first document of the ISR etc.

2. The priority document pertaining to the present application was not available at the time of establishing this IPER. Hence, the current assessment is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, document WO-A-9739119 cited as D4 in the ISR could become relevant to assess whether the subject matter of the present application satisfies the criteria set forth in Article 33(1) PCT.

Additional remarks to section III:

The ISR has been performed only on the subject matter relating to the nucleotide sequence of SEQ ID NO:1. Therefore this IPER has been performed on said subject matter only: claims 1-17 and 19-26 partially insofar as they relate to SEQ ID NO:1. Claims 18, 27 and 29 relate to sequences other than SEQ ID NO: 1. Claim 28 is a general claim which relates to gene products whose over expression inhibit reproduction of the virus. The polypeptide encoded by SEQ ID NO: 1 is a polypeptide necessary for reproduction of the virus in the cell. Thus it seems that also claim 28 does not relate to SEQ ID NO: 1.

Additional remarks to section V:

1. Novelty and Inventive step (Article 33(2) and (3) PCT)

The present application relates to nucleic acids encoding gene products used for viral infection, but which are not essential for cell survival.

Document D1 discloses a method to identify genes that are involved in viral infection, but does not disclose the nucleic acid of SEQ ID NO:1 of the present

application. D2 and D3 both disclose genes and their encoded proteins, which are involved in the replication and propagation of a virus in the cell. The genes disclosed in D2, human creatine kinase B and adenosine deaminase, are involved in purine metabolism and thus have an essential cellular function. The gene disclosed in D3, TRP-185, is indicated to be expected to be important in the regulation of cellular genes (as well as viral genes). Therefore the cited prior art does not disclose nor suggest any sequence encoding a gene product that is essential for viral infection but not essential for cell survival. The prior art certainly does not disclose nor suggest a nucleic acid having the sequence of SEQ ID NO:1. Thus, claims 1-17 and 19-26, insofar as they relate to SEQ ID NO:1, are considered novel and inventive.

2. Industrial applicability (Article 33(4) PCT)

The subject matter of claims 1-16 and 24-26 is considered industrially applicable. For the assessment of present claims 17 and 19-23 on the question whether they are industrially applicable, no unified criteria exist in PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment. The applicant is already informed that in the case of a European application, claims 17 and 19-23 are not allowable because 'methods of treatment of the human or animal body by surgery or by therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application'. Claims 20-23, although relating to mutating the gene comprising SEQ ID NO: 1 ***ex vivo***, they refer to a method which includes '**placing the cell in the subject**' (e.g. a human subject, claim 22) and thus involves a method of treatment of the human or animal body.

Additional remarks to section VIII:

The following objections are raised under **Article 6 PCT** concerning the clarity of the

claims:

1. The subject matter of claims 5, 15, 17, 20, 24 and 26 lacks clarity in that the term '**homolog**' is not suitable to define clearly the scope of the claims: in the absence of the specification that the homolog has the same function as the gene product of SEQ ID NO: 1, a homolog could be a nucleic acid encoding a polypeptide with any amount of homology performing any function. In view of the description (p. 9 and 10), a homolog could have from 50 to 98% homology. It is questionable whether a nucleic acid with only 50% homology would encode a protein with the same function. In addition the description (p. 10, l. 12-13) indicates that a homolog can be confirmed as a homolog by its functionality, implying that not every homolog necessarily has the same function.
   The same objection seems to apply to the term '**homology**' in claims 8-13, which appears unclear in the absence of a functional limitation.

2. The subject matter of claim 7 lacks clarity in that the wording '**selectively hybridizes under stringent conditions**' is not suitable to define clearly the scope of the claim. The hybridization conditions are not specified and thus appear to include e.g. low stringency conditions, under which conditions any unrelated nucleic acid could hybridize. In the absence of a functional limitation the subject matter of claim 7 encompasses many nucleic acids encoding polypeptides that are functionally unrelated to the polypeptide of the present invention (encoded by SEQ ID NO: 1).

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C12N 15/12, 15/11, 15/10, C07K 14/47, C12Q 1/68, G01N 33/50, 33/574

A3

(11) International Publication Number: **WO 99/19481**

(43) International Publication Date: 22 April 1999 (22.04.99)

(21) International Application Number: PCT/US98/21276

(22) International Filing Date: 8 October 1998 (08.10.98)

(30) Priority Data:
60/062,021 10 October 1997 (10.10.97) US

(71) Applicant *(for all designated States except US)*: VANDERBILT UNIVERSITY [US/US]; 305 Kirkland Hall, Nashville, TN 37240 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: RUBIN, Donald, H. [US/US]; 1937 Edenbridge Way, Nashville, TN 37215 (US). ORGAN, Edward, L. [US/US]; 2505 Essex Place, Nashville, TN 37202 (US). DUBOIS, Raymond, N. [US/US]; 281 St. Andrew Drive, Franklin, TN 37064 (US).

(74) Agents: KIMPEL, Janice, A. et al.; Needle & Rosenberg, P.C., 127 Peachtree Street, N.E., Atlanta, GA 30303 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
4 November 1999 (04.11.99)

(54) Title: MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION

(57) **Abstract**

The present invention provides methods of identifying cellular genes necessary for viral growth and cellular genes that function as tumor suppressors. Thus, the present invention provides nucleic acids related to and methods of reducing or preventing viral infection or cancer. The invention also provides methods of producing substantially virus–free cell cultures and methods for screening for additional such genes.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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09/509712

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
22000.0086/P		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 98/21276	08/10/1998	10/10/1997
Applicant		
VANDERBILT UNIVERSITY et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   ☒ contained in the international application in written form.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readble form.

   ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   ☒ the text is approved as submitted by the applicant.

   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   ☒ the text is approved as submitted by the applicant.

   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. --

   ☐ as suggested by the applicant.

   ☐ because the applicant failed to suggest a figure.

   ☐ because this figure better characterizes the invention.

   ☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 98/21276

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 17-19 and 27 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-29 (partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: (1-29) partially

An isolated nucleic acid comprising a nucleotide sequence SEQ ID NO.1; a host cell containing said sequence; a polypeptide comprising the amino acid sequence encoded by said nucleic acid sequence; a nucleic acid comprising a regulatory region of a gene comprising the nucleotide sequence SEQ ID NO.1; a method of reducing or inhibiting a viral infection and/or suppressing a malignant phenotype in a subject and/or cell, comprising administering to a subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid sequence SEQ ID NO.1; a method of reducing or inhibiting a viral infection comprising mutating ex vivo in a selected cell an endogenous gene comprising the nucleic acid SEQ ID NO.1; a method of screening a compound for effectiveness in treating or preventing a viral infection, and/or that can suppress a malignant phenotype in a subject and/or cell, comprising administering the compound to a cell containing a cellular gene and/or nucleic acid functionally encoding a gene product encoded by a gene comprising the the nucleic acid SEQ ID NO.1; a method of screening a compound for effectiveness in treating or preventing a viral infection, comprising contacting the compound with the gene product of a cellular gene comprising nucleic acid SEQ ID NO.1; a method for suppressing a malignant phenotype in a cell in a subject, comprising administering the compound to a cell containing a cellular gene product encoded by a gene comprising the nucleic acid sequence SEQ ID NO.1 whose overexpression inhibits reproduction of the virus but does not prevent survival of the cell and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for treating the viral infection;

2. Claims: (1-29) patially

Idem as subject 1 , but limited to and as far as applicable to SEQ ID NOs.2-127. (Subject 2 is limited to SEQ ID NO.2; Subject 3 is limited to SEQ ID NO.3; ....Subject 127 is limited to SEQ ID NO.127).

INTERNATIONAL SEARCH REPORT

Internatio ‹pplication No
PCT/US 98/21276

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C12N15/11 C12N15/10 C07K14/47 C12Q1/68
G01N33/50 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	E. ORGAN ET AL.: "U3 gene-trap retrovirus selection of cellular mutants resistant to lytic reovirus infection" J. INVESTIGATIVE MEDICINE, ISSN: 1081-5589,, vol. 44, no. 3, March 1996, page 320A XP002090533 Annual Meeting of the Association of American Physicians, The American Society for Clinical Investigation, and the American Federation for Clinical Research: Biomedicine '96, Medical Research from Bench to Bedside Washington, D.C., USA May 3-6, 1996,	1-15
Y	see Abstract on p320A, left col., 2nd Par.;	27,29

	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 January 1999	24. 09. 1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	HORNIG H.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Internatic application No
PCT/US 98/21276

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 90 09192 A (MASSACHUSETTS INST TECHNOLOGY ;UNIV HARVARD (US)) 23 August 1990 see the whole document	27,29
Y	WO 93 09230 A (UNIV TEXAS) 13 May 1993 see the whole document	27,29
P,A	WO 97 39119 A (ORGAN EDWARD L ;RUBIN DONALD H (US); UNIV VANDERBILT (US); DUBOIS) 23 October 1997 see the whole document	1-29
A	US 5 627 058 A (RULEY H EARL ET AL) 6 May 1997 see the whole document	1-29
A	SKARNES W C: "THE IDENTIFICATION OF NEW GENES: GENE TRAPPING IN TRANSGENIC MICE" CURRENT OPINION IN BIOTECHNOLOGY, vol. 4, 1 January 1993, pages 684-689, XP000569473 see the whole document	1-29
A	EVANS M J ET AL: "Gene trapping and functional genomics" TRENDS IN GENETICS, vol. 13, no. 9, September 1997, page 370-374 XP004086832 see the whole document	1-29

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 98/21276

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 17-19 and 27 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-29 (partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 98/21276

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: (1-29) partially

An isolated nucleic acid comprising a nucleotide sequence SEQ ID NO.1; a host cell containing said sequence; a polypeptide comprising the amino acid sequence encoded by said nucleic acid sequence; a nucleic acid comprising a regulatory region of a gene comprising the nucleotide sequence SEQ ID NO.1; a method of reducing or inhibiting a viral infection and/or suppressing a malignant phenotype in a subject and/or cell, comprising administering to a subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid sequence SEQ ID NO.1; a method of reducing or inhibiting a viral infection comprising mutating ex vivo in a selected cell an endogenous gene comprising the nucleic acid SEQ ID NO.1; a method of screening a compound for effectiveness in treating or preventing a viral infection, and/or that can suppress a malignant phenotype in a subject and/or cell, comprising administering the compound to a cell containing a cellular gene and/or nucleic acid functionally encoding a gene product encoded by a gene comprising the the nucleic acid SEQ ID NO.1; a method of screening a compound for effectiveness in treating or preventing a viral infection, comprising contacting the compound with the gene product of a cellular gene comprising nucleic acid SEQ ID NO.1; a method for suppressing a malignant phenotype in a cell in a subject, comprising administering the compound to a cell containing a cellular gene product encoded by a gene comprising the nucleic acid sequence SEQ ID NO.1 whose overexpression inhibits reproduction of the virus but does not prevent survival of the cell and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for treating the viral infection;

2. Claims: (1-29) patially

Idem as subject 1 , but limited to and as far as applicable to SEQ ID NOs.2-127. (Subject 2 is limited to SEQ ID NO.2; Subject 3 is limited to SEQ ID NO.3; ....Subject 127 is limited to SEQ ID NO.127).

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internatic Application No
PCT/US 98/21276

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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